## Arguments/Remarks

Claims 2 and 4-6 are pending in the application. Claims 2, 4 and 5 have been amended. Claims 1, 3, and 7-11 have been cancelled in this or a prior amendment without disclaimer or prejudice. No new matter has been introduced by the instant claims. Applicants reserve the right to pursue the subject matter cancelled in this or a subsequent application.

### I. Rejection of claims 1-3, 5 and 6 under 35 U.S.C. § 112, first paragraph

Claims 1-3, 5 and 6 stand rejected under §112, first paragraph, as failing to comply with the written description requirement.

Claim 2 has been amended to particularly define the substituents at the $R^{3'}$ and $R^{6'}$ positions based on the compounds exemplified in the specification of the instant application.

Thus, the claims as currently amended satisfy the written description requirement of §112, first paragraph.

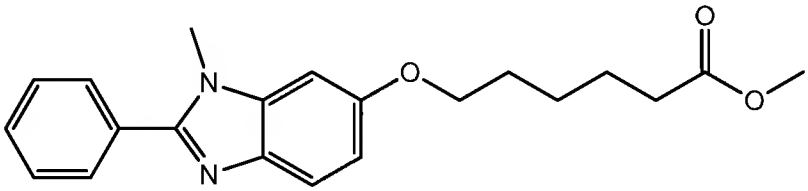
### II. Rejection of claims 1-6 under 35 U.S.C. § 103

Claims 1-6 stand rejected under §103 as being unpatentable over U.S. Patent 6,855,714 (Blume) in view of G. Patani & E. LaVoie *Bioisosterism: A rational Approach in Drug Design,* 96 Chem. Rev. 3147 (1996) (Patani).

As the Blume patent is understood, a genus of benzimdazoles are disclosed, which compounds are trisubstituted at the 1, 2, and either 5 or 6 position of the benzimidazole ring system. The disclosed compounds are allegedly efficacious in preventing diseases associated with microglia activation (e.g., Alzheimer's Disease, and related neurodegenerative diseases).

As noted by the Examiner, Blume discloses 113 species at columns 19 to 24. Each of these species is mono-substituted on the benzo ring of the benzimidazole ring system. More particularly, each of the disclosed compounds is mono substituted at the 5 or 6 position of the benzimidazole ring system with a substituted pentyloxy substitutent. The compound of Example 4 is representative:

None of the compounds disclosed by Blume are substituted on the benzene ring ortho to the fused imidazole ring, e.g., at the positions corresponding to R3 and R6 of the formula I of claim 1 of the instant application.



In contrast, claim 2, as currently amended, is directed to compounds in which the benzimidazole is substituted at both the 4 and 7 position (e.g., $R^{3'}$ and $R^{6'}$). In addition, compounds having an alkoxy residue at either of the 5 or 6 position of the benzimidazole are excluded from the scope of the currently amended claims. Claim 4 is directed to a Markush group of chemical species, each of which comprises non-hydrogen substituents at the 4 and 7 position of the benzimidazole ring. None of the species of claim 4 include a substituted alkoxy at either the 5 or 6 position of benzimidazole ring.

One of ordinary skill in the art would have neither motivation nor an expectation of obtaining compounds which retain microglial inhibitory activity by deletion of a conserved functional group present in every compound disclosed in the Blume patent. More particularly, one of skill in the art would not have motivation to delete or modify the substituted pentyloxy substituent at the 6 position of the benzimidazole core.

The Patani teaching of bioisosterism fails to supply a basis for the deletion of the apparently essential substituted pentyloxy substituent present in all of the Blume benzimidazole compounds.

The office action requires substantial contortions to obtain the compounds of the instantly claimed invention from the disclosure of Blume. In particular, the 6-pentyloxy substituent of Blume must be deleted, multiple hydrogen atoms must be replaced with non-hydrogen substituents in order to the compounds of the invention. Nowhere does the Office Action assert any motivation to make the necessary changes nor is there any suggestion from the cited art documents that such a particular combination of modifications would provide effective microglial inhibitors

Claim 4, as currently amended, is an independent claim directed to a plurality of benzimidazole species, each of which is di substituted on the benzene ring ortho to the fused imidazole ring and none of which comprise a subsituted alkoxy substituent at either the 5 or 6 position of the benzimidazole ring. The Office Action has failed to provide any basis to make the necessary changes to the compounds disclosed in Blume to reach the particular species provided by claim 4.

Absent of a showing of any motivation to make the multiple changes to the compounds disclosed in Blume, the Office Action has failed to establish a *prima facie* case of obviousness. Applicants request withdrawal of the rejection and reconsideration of the claims.

Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,

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Date: 15 April 2011